

SEQUENCE LISTING



11

17

<110> Lim, Moon Young Edwards, Cynthia A. Fry, Kirk E. Bruice, Thomas W. Starr, Douglas B. Laurance, Megan E. Kwok, Yan

<120> DNA Binding Compound-Mediated Molecular Switch System

- <130> 4600-0130.30
- <140> US 09/518,297
- <141> 2000-03-03
- <150> US 60/122,513
- <151> 1999-03-03
- <150> US 60/154,605
- <151> 1999-09-17
- <160> 62
- <170> FastSEQ for Windows Version 4.0
- <210> 1
- <211> 11
- <212> DNA
- <213> Artificial Sequence
- <220>
- <223> DNA response element
- <400> 1

cgttcgcact t

- <210> 2
- <211> 17
- <212> DNA
- <213> Artificial Sequence
- <220>
- <223> DNA response element
- <400> 2
- cggagtactg tcctccg
- <210> 3
- <211> 12
- <212> DNA
- <213> Artificial Sequence

```
<220>
<223> DNA response element
<221> misc feature
<222> (1)...(12)
<223> n = A, T, C or G
<400> 3
taattanggg ng
<210> 4
<211> 551
<212> PRT
<213> Homo sapiens
<220>
<221> VARIANT
<222> (0)...(0)
<223> transcriptional regulatory protein
<400> 4
Met Asp Glu Leu Phe Pro Leu Ile Phe Pro Ala Glu Pro Ala Gln Ala
Ser Gly Pro Tyr Val Glu Ile Ile Glu Gln Pro Lys Gln Arg Gly Met
Arg Phe Arg Tyr Lys Cys Glu Gly Arg Ser Ala Gly Ser Ile Pro Gly
                            40
Glu Arg Ser Thr Asp Thr Thr Lys Thr His Pro Thr Ile Lys Ile Asn
Gly Tyr Thr Gly Pro Gly Thr Val Arg Ile Ser Leu Val Thr Lys Asp
                    70
                                        75
Pro Pro His Arg Pro His Pro His Glu Leu Val Gly Lys Asp Cys Arg
                                    90
Asp Gly Phe Tyr Glu Ala Glu Leu Cys Pro Asp Arg Cys Ile His Ser
            100
                                105
Phe Gln Asn Leu Gly Ile Gln Cys Val Lys Lys Arg Asp Leu Glu Gln
                            120
Ala Ile Ser Gln Arg Ile Gln Thr Asn Asn Pro Phe Gln Val Pro
                        135
                                            140
Ile Glu Glu Gln Arg Gly Asp Tyr Asp Leu Asn Ala Val Arg Leu Cys
                    150
                                        155
Phe Gln Val Thr Val Arg Asp Pro Ser Gly Arg Pro Leu Arg Leu Pro
                165
                                    170
Pro Val Leu Pro His Pro Ile Phe Asp Asn Arg Ala Pro Asn Thr Ala
                                185
Glu Leu Lys Ile Cys Arg Val Asn Arg Asn Ser Gly Ser Cys Leu Gly
                            200
Gly Asp Glu Ile Phe Leu Leu Cys Asp Lys Val Gln Lys Glu Asp Ile
                        215
                                            220
Glu Val Tyr Phe Thr Gly Pro Gly Trp Glu Ala Arg Gly Ser Phe Ser
                    230
                                        235
Gln Ala Asp Val His Arg Gln Val Ala Ile Val Phe Arg Thr Pro Pro
                245
                                    250
Tyr Ala Asp Pro Ser Leu Gln Ala Pro Val Arg Val Ser Met Gln Leu
                               265
Arg Arg Pro Ser Asp Arg Glu Leu Ser Glu Pro Met Glu Phe Gln Tyr
```

12

280

```
Leu Pro Asp Thr Asp Asp Arg His Arg Ile Glu Glu Lys Arg Lys Arg
                        295
                                            300
Thr Tyr Glu Thr Phe Lys Ser Ile Met Lys Lys Ser Pro Phe Ser Gly
                                       315
                   310
Pro Thr Asp Pro Arg Pro Pro Pro Arg Arg Ile Ala Val Pro Ser Arg
               325
                                    330
Ser Ser Ala Ser Val Pro Lys Pro Ala Pro Gln Pro Tyr Pro Phe Thr
                                345
Ser Ser Leu Ser Thr Ile Asn Tyr Asp Glu Phe Pro Thr Met Val Phe
                            360
Pro Ser Gly Gln Ile Ser Gln Ala Ser Ala Leu Ala Pro Ala Pro Pro
                        375
                                            380
Gln Val Leu Pro Gln Ala Pro Ala Pro Ala Pro Ala Pro Ala Met Val
                    390
                                        395
Ser Ala Leu Ala Gln Ala Pro Ala Pro Val Pro Val Leu Ala Pro Gly
                405
                                    410
Pro Pro Gln Ala Val Ala Pro Pro Ala Pro Lys Pro Thr Gln Ala Gly
           420
                                425
                                                    430
Glu Gly Thr Leu Ser Glu Ala Leu Leu Gln Leu Gln Phe Asp Asp Glu
                           440
Asp Leu Gly Ala Leu Leu Gly Asn Ser Thr Asp Pro Ala Val Phe Thr
                        455
                                            460
Asp Leu Ala Ser Val Asp Asn Ser Glu Phe Gln Gln Leu Leu Asn Gln
                    470
                                        475
Gly Ile Pro Val Ala Pro His Thr Thr Glu Pro Met Leu Met Glu Tyr
                485
                                    490
Pro Glu Ala Ile Thr Arg Leu Val Thr Gly Ala Gln Arg Pro Pro Asp
                                505
Pro Ala Pro Ala Pro Leu Gly Ala Pro Gly Leu Pro Asn Gly Leu Leu
                           520
                                                525
Ser Gly Asp Glu Asp Phe Ser Ser Ile Ala Asp Met Asp Phe Ser Ala
                        535
Leu Leu Ser Gln Ile Ser Ser
                    550
<210> 5
<211> 19
<212> DNA
<213> Artificial Sequence
<220>
<223> DNA response element
<400> 5
tccctatcag tgatagaga
                                                                        19
<210> 6
<211> 22
<212> DNA
<213> Artificial Sequence
<223> response element
<400> 6
                                                                        22
```

cttaacactc gcgagtgtta ag

```
<210> 7
<211> 13
<212> DNA
<213> Artificial Sequence
<220>
<223> response element
<221> misc feature
<222> (3)...(3)
<223> n = G \text{ or } T
<221> misc_feature
<222> (7)...(7)
<223> n = A, T, C \text{ or } G
<221> misc feature
<222> (12)...(12)
<223> n = A or C
<400> 7
rgntcantga cny
                                                                         13
<210> 8
<211> 77
<212> PRT
<213> Artificial Sequence
<220>
<223> activator sequence
<400> 8
Ala Pro Pro Thr Asp Val Ser Leu Gly Asp Glu Leu His Leu Asp Gly
1
                 5
                                      10
Glu Asp Val Ala Met Ala His Ala Asp Ala Leu Asp Asp Phe Asp Leu
Asp Met Leu Gly Asp Gly Asp Ser Pro Gly Pro Gly Phe Thr Pro His
Asp Ser Ala Pro Tyr Gly Ala Leu Asp Met Ala Asp Phe Glu Phe Glu
                         55
Gln Met Phe Thr Asp Ala Leu Gly Ile Asp Glu Tyr Gly
                     70
<210> 9
<211> 11
<212> PRT
<213> Artificial Sequence
<220>
<223> activator sequence
<221> VARIANT
<222> (1)...(11)
<223> tetramer
<400> 9
```

Asp Ala Leu Asp Asp Phe Asp Leu Asp Met Leu

```
1
                                   10
<210> 10
<211> 97
<212> PRT
<213> Artificial Sequence
<223> repressor sequence
Met Asp Ala Lys Ser Leu Thr Ala Trp Ser Arg Thr Leu Val Thr Phe
                                    10
Lys Asp Val Phe Val Asp Phe Thr Arg Glu Glu Trp Lys Leu Leu Asp
                                25
Thr Ala Gln Gln Ile Val Tyr Arg Asn Val Met Leu Glu Asn Tyr Lys
                            40
Asn Leu Val Ser Leu Gly Tyr Gln Leu Thr Lys Pro Asp Val Ile Leu
                        55
                                             60
Arg Leu Glu Lys Gly Glu Glu Pro Trp Leu Val Glu Arg Glu Ile His
                    70
                                        75
Gln Glu Thr His Pro Asp Ser Glu Thr Ala Phe Glu Ile Lys Ser Ser
                85
Val
<210> 11
<211> 36
<212> PRT
<213> Artificial Sequence
<220>
<223> repressor sequence
<400> 11
Met Ala Ala Val Arg Met Asn Ile Gln Met Leu Leu Glu Ala Ala
                                    10
Asp Tyr Leu Glu Arg Arg Glu Arg Glu Ala Glu His Gly Tyr Ala Ser
                                25
                                                     30
Met Leu Pro Tyr
        35
<210> 12
<211> 116
<212> DNA
<213> Escherichia coli
<220>
<221> misc feature
<222> (0) ... (0)
<223> partial promoter sequence
<400> 12
cgcggtcaga aaattatttt aaatttcctc ttgtcaggcc ggaataactc cctataatgc
                                                                        60
gccaccactg acacggaaca acggcaaaca cgccqccqqq tcagcqqqqt tctcct
                                                                       116
```

<210> 13

<211> 22	
<212> DNA	
<213> Escherichia coli	
V2137 BSCHEFFCHTA COTT	
<220>	
<221> misc_feature	
<222> (0) (0)	
<223> partial promoter sequence	
1223 paretar promoter begaenee	
4400- 13	
<400> 13	
agaaaattat tttaaatttc ct	22
<210> 14	
<211> 22	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> modified promoter sequence	
•	
<400> 14	
	22
gactgcagtg gtacctagga gg	22
<210> 15	
<211> 22	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> modified promoter sequence	
<400> 15	
agaaaattat tttaaatttc ct	22
-	
<210> 16	
<211> 22	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> modified promoter sequence	
modeled bedween	
<400> 16	
ggaaaatttt ttttcaaaag ta	22
<210> 17	
<211> 22	
<212> DNA	
<213> Artificial Sequence	
7210/ MICHITCIAL Sequence	
.000	
<220>	
<223> modified promoter sequence	
• • • • • • • • • • • • • • • • • • •	
<400> 17	
	22
tgaaatttat tttgcgaaag gg	22
∠210 \ 10	

```
<211> 11
<212> DNA
<213> Artificial Sequence
<220>
<223> engineered DNA response element
<400> 18
tgttcgcact t
                                                                         11
<210> 19
<211> 52
<212> DNA
<213> Artificial Sequence
<220>
<223> engineered DNA response element
catggacgcc actgagccgt ttttgttcgc acttgaggcg agtcgatgca cc
                                                                         52
<210> 20
<211> 54
<212> DNA
<213> Artificial Sequence
<220>
<223> engineered DNA response element
catggacgcc actgagccgt gttcgcactt ttttttgagg cgagtcgatg cacc
                                                                         54
<210> 21
<211> 58
<212> DNA
<213> Artificial Sequence
<220>
<223> engineered DNA response element
catggacgcc actgagccgt ttttgttcgc acttttttt gaggcgagtc gatgcacc
                                                                         58
<210> 22
<211> 12
<212> DNA
<213> Artificial Sequence
<220>
<223> engineered DNA response element
<400> 22
cttaaaaata ac
                                                                         12
<210> 23
<211> 16
<212> DNA
```

<pre><220> <223> engineered DNA response element <400> 23 ttgaaaaatc aacgct</pre>
<pre><400> 23 ttgaaaaatc aacgct</pre>
ttgaaaaatc aacgct <210> 24 <211> 21 <212> DNA <213> Artificial Sequence <220> <223> engineered DNA response element <400> 24 tttttgttcg cactttttt t <210> 25 <211> 20 <212> DNA <213> Artificial Sequence
<pre><210> 24 <211> 21 <212> DNA <213> Artificial Sequence <220> <223> engineered DNA response element <400> 24 tttttgttcg cactttttt t <210> 25 <211> 20 <212> DNA <213> Artificial Sequence</pre>
<pre><211> 21 <212> DNA <213> Artificial Sequence <220> <223> engineered DNA response element <400> 24 tttttgttcg cactttttt t <210> 25 <211> 20 <212> DNA <213> Artificial Sequence</pre>
<212> DNA <213> Artificial Sequence <220> <223> engineered DNA response element <400> 24 tttttgttcg cactttttt t <210> 25 <211> 20 <212> DNA <213> Artificial Sequence
<213> Artificial Sequence <220> <223> engineered DNA response element <400> 24 tttttgttcg cactttttt t 21 <210> 25 <211> 20 <212> DNA <213> Artificial Sequence
<223> engineered DNA response element <400> 24 tttttgttcg cactttttt t 21 <210> 25 <211> 20 <212> DNA <213> Artificial Sequence
<223> engineered DNA response element <400> 24 tttttgttcg cactttttt t 21 <210> 25 <211> 20 <212> DNA <213> Artificial Sequence
tttttgttcg cactttttt t <210> 25 <211> 20 <212> DNA <213> Artificial Sequence
<210> 25 <211> 20 <212> DNA <213> Artificial Sequence
<211> 20 <212> DNA <213> Artificial Sequence
<212> DNA <213> Artificial Sequence
<213> Artificial Sequence
<220>
<223> engineered DNA response element
<400> 25 tttttgggat tttccttttt 20
<210> 26
<211> 28
<212> DNA
<213> Artificial Sequence
<220>
<223> engineered DNA response element
<400> 26 aaaaaattgt gagcgctcac aatttttt 28
aaaaaattgt gagcgctcac aatttttt 28
<210> 27
<211> 6 <212> DNA
<213> Artificial Sequence
<220>
<223> tissue-specific transcription factor
<400> 27
acttta
<210> 28
<211> 9 <212> DNA
<213> Artificial Sequence

<220> <223>	engineered DNA response element	
<400> taccga		9
<210> <211> <212> <213>	10	
<220> <223>	engineered DNA response element	
<400> gggact		10
<210> <211> <212> <213>	10	
<220> <223>	engineered DNA response element	
<400>		10
<210> <211> <211> <212> <213> <	50	
<220> <223>	engineered DNA response element	
<400> :	* -	50
<210> 3 <211> 3 <212> 1 <213> 2	50	
<220> <223>	engineered DNA response element	
<400> : cgaccg		50
<210> 3 <211> 3 <212> 1 <213> 2	50	
<220>	engineered DNA response element	

<400> cgacco		aattg ggatttt	сса	aaaacgatc	g gac	tggact	С	50
<210> <211> <212> <213>	28	Sequence						
<220> <223>	engineered	DNA response	ele	ment				
<400> aaaaaa	=	ctcac aatttt	t					28
<210><211><212><212><213>	25	Sequence						
<220> <223>	engineered	DNA response	ele	ment				
<400> tttttt	35 ttgt gageg	gataa caaaa						25
<210><211><212><212><213>	10	Sequence						
<220> <223>	engineered	DNA response	ele	ment				
<400> tctggg								10
<210><211><211><212><213>	14	Sequence						
<220> <223>	engineered	DNA response	eler	ment				
<400> gagttt	37 tttt taag							14
<210> <211> <212> <213>	14	Sequence						
<220> <223>	engineered	DNA response	eler	ment				
<100×	20							

qagttttaaa agag 14

```
<210> 39
<211> 969
<212> PRT
<213> Homo sapiens
<220>
<221> VARIANT
<222> (0)...(0)
<223> transcriptional regulatory protein
<400> 39
Met Ala Glu Asp Asp Pro Tyr Leu Gly Arg Pro Glu Gln Met Phe His
Leu Asp Pro Ser Leu Thr His Thr Ile Phe Asn Pro Glu Val Phe Gln
           20
                                25
Pro Gln Met Ala Leu Pro Thr Ala Asp Gly Pro Tyr Leu Gln Ile Leu
                            40
                                                45
Glu Gln Pro Lys Gln Arg Gly Phe Arg Phe Arg Tyr Val Cys Glu Gly
                        55
Pro Ser His Gly Gly Leu Pro Gly Ala Ser Ser Glu Lys Asn Lys Lys
                                        75
                    70
Ser Tyr Pro Gln Val Lys Ile Cys Asn Tyr Val Gly Pro Ala Lys Val
                                    90
Ile Val Gln Leu Val Thr Asn Gly Lys Asn Ile His Leu His Ala His
                               105
           100
Ser Leu Val Gly Lys His Cys Glu Asp Gly Ile Cys Thr Val Thr Ala
                           120
Gly Pro Lys Asp Met Val Val Gly Phe Ala Asn Leu Gly Ile Leu His
                        135
                                            140
Val Thr Lys Lys Lys Val Phe Glu Thr Leu Glu Ala Arg Met Thr Glu
                   150
                                       155
Ala Cys Ile Arg Gly Tyr Asn Pro Gly Leu Leu Val His Pro Asp Leu
                                   170
               165
Ala Tyr Leu Gln Ala Glu Gly Gly Asp Arg Gln Leu Gly Asp Arg
                               185
           180
Glu Lys Glu Leu Ile Arg Gln Ala Ala Leu Gln Gln Thr Lys Glu Met
                            200
Asp Leu Ser Val Val Arg Leu Met Phe Thr Ala Phe Leu Pro Asp Ser
                       215
                                            220
Thr Gly Ser Phe Thr Arg Arg Leu Glu Pro Val Val Ser Asp Ala Ile
                   230
                                       235
Tyr Asp Ser Lys Ala Pro Asn Ala Ser Asn Leu Lys Ile Val Arg Met
                                   250
               245
Asp Arg Thr Ala Gly Cys Val Thr Gly Gly Glu Glu Ile Tyr Leu Leu
           260
                                265
                                                    270
Cys Asp Lys Val Gln Lys Asp Asp Ile Gln Ile Arg Phe Tyr Glu Glu
                           280
                                                285
Glu Glu Asn Gly Gly Val Trp Glu Gly Phe Gly Asp Phe Ser Pro Thr
                       295
                                            300
Asp Val His Arg Gln Phe Ala Ile Val Phe Lys Thr Pro Lys Tyr Lys
                    310
                                        315
Asp Ile Asn Ile Thr Lys Pro Ala Ser Val Phe Val Gln Leu Arg Arg
               325
                                   330
Lys Ser Asp Leu Glu Thr Ser Glu Pro Lys Pro Phe Leu Tyr Tyr Pro
```

345

```
Glu Ile Lys Asp Lys Glu Glu Val Gln Arg Lys Arg Gln Lys Leu Met
                           360
Pro Asn Phe Ser Asp Ser Phe Gly Gly Gly Ser Gly Ala Gly Ala Gly
                       375
                                           380
Gly Gly Gly Met Phe Gly Ser Gly Gly Gly Gly Gly Thr Gly Ser
                   390
                                       395
Thr Gly Pro Gly Tyr Ser Phe Pro His Tyr Gly Phe Pro Thr Tyr Gly
               405
                                  410
Gly Ile Thr Phe His Pro Gly Thr Thr Lys Ser Asn Ala Gly Met Lys
                               425
His Gly Thr Met Asp Thr Glu Ser Lys Asp Pro Glu Gly Cys Asp
                           440
Lys Ser Asp Asp Lys Asn Thr Val Asn Leu Phe Gly Lys Val Ile Glu
                       455
                                           460
Thr Thr Glu Gln Asp Gln Glu Pro Ser Glu Ala Thr Val Gly Asn Gly
                  470
                                       475
Glu Val Thr Leu Thr Tyr Ala Thr Gly Thr Lys Glu Glu Ser Ala Gly
               485
                                   490
Val Gln Asp Asn Leu Phe Leu Glu Lys Ala Met Gln Leu Ala Lys Arg
           500
                               505
His Ala Asn Ala Leu Phe Asp Tyr Ala Val Thr Gly Asp Val Lys Met
                           520
Leu Leu Ala Val Gln Arg His Leu Thr Ala Val Gln Asp Glu Asn Gly
                       535
                                           540
Asp Ser Val Leu His Leu Ala Ile Ile His Leu His Ser Gln Leu Val
                   550
                                       555
Arg Asp Leu Leu Glu Val Thr Ser Gly Leu Ile Ser Asp Asp Ile Ile
               565
                                   570
Asn Met Arg Asn Asp Leu Tyr Gln Thr Pro Leu His Leu Ala Val Ile
                               585
Thr Lys Gln Glu Asp Val Val Glu Asp Leu Leu Arg Ala Gly Ala Asp
                           600
                                              605
Leu Ser Leu Leu Asp Arg Leu Gly Asn Ser Val Leu His Leu Ala Ala
                       615
                                           620
Lys Glu Gly His Asp Lys Val Leu Ser Ile Leu Leu Lys His Lys Lys
                   630
                                       635
Ala Ala Leu Leu Asp His Pro Asn Gly Asp Gly Leu Asn Ala Ile
                                   650
               645
His Leu Ala Met Met Ser Asn Ser Leu Pro Cys Leu Leu Leu Val
                               665
Ala Ala Gly Ala Asp Val Asn Ala Gln Glu Gln Lys Ser Gly Arg Thr
                           680
Ala Leu His Leu Ala Val Glu His Asp Asn Ile Ser Leu Ala Gly Cys
                       695
Leu Leu Glu Gly Asp Ala His Val Asp Ser Thr Thr Tyr Asp Gly
                   710
                                       715
Thr Thr Pro Leu His Ile Ala Ala Gly Arg Gly Ser Thr Arg Leu Ala
                                   730
               725
Ala Leu Leu Lys Ala Ala Gly Ala Asp Pro Leu Val Glu Asn Phe Glu
           740
                               745
Pro Leu Tyr Asp Leu Asp Asp Ser Trp Glu Asn Ala Gly Glu Asp Glu
                           760
Gly Val Val Pro Gly Thr Thr Pro Leu Asp Met Ala Thr Ser Trp Gln
                       775
                                           780
Val Phe Asp Ile Leu Asn Gly Lys Pro Tyr Glu Pro Glu Phe Thr Ser
                  790
                              795
Asp Asp Leu Leu Ala Gln Gly Asp Met Lys Gln Leu Ala Glu Asp Val
```

```
805
                                     810
                                                         815
Lys Leu Gln Leu Tyr Lys Leu Leu Glu Ile Pro Asp Pro Asp Lys Asn
                                 825
Trp Ala Thr Leu Ala Gln Lys Leu Gly Leu Gly Ile Leu Asn Asn Ala
                             840
Phe Arg Leu Ser Pro Ala Pro Ser Lys Thr Leu Met Asp Asn Tyr Glu
    850
                        855
                                             860
Val Ser Gly Gly Thr Val Arg Glu Leu Val Glu Ala Leu Arg Gln Met
                    870
                                         875
Gly Tyr Thr Glu Ala Ile Glu Val Ile Gln Ala Ala Ser Ser Pro Val
                                     890
                885
Lys Thr Thr Ser Gln Ala His Ser Leu Pro Leu Ser Pro Ala Ser Thr
            900
                                 905
                                                     910
Arg Gln Gln Ile Asp Glu Leu Arg Asp Ser Asp Ser Val Cys Asp Thr
                             920
Gly Val Glu Thr Ser Phe Arg Lys Leu Ser Phe Thr Glu Ser Leu Thr
                        935
                                             940
Ser Gly Ala Ser Leu Leu Thr Leu Asn Lys Met Pro His Asp Tyr Gly
                    950
                                         955
Gln Glu Gly Pro Leu Glu Gly Lys Ile
                965
<210> 40
<211> 96
<212> DNA
<213> Artificial Sequence
<220>
<223> engineered regulatory sequence
<400> 40
gctagccccg ccccgttgac gcaaatgggc ggtaggcgtg tacggtggga ggtttatata
                                                                         60
agcagagete gtttagtgaa cegteagate agatet
                                                                         96
<210> 41
<211> 154
<212> DNA
<213> Artificial Sequence
<220>
<223> engineered regulatory sequence
<400> 41
gctagcgccc aaattgggat tttccaaaaa gccgaaattg ggattttcca aaaaccgccg
                                                                         60
atcgcccgcc ccgttgacgc aaatgggcgg taggcgtgta cggtgggagg tttatataag
                                                                        120
cagagetegt ttagtgaace gteagateag atet
                                                                        154
<210> 42
<211> 212
<212> DNA
<213> Artificial Sequence
<220>
<223> engineered regulatory sequence
<400> 42
acgcgtgccc aaattgggat tttccaaaaa gccgaaattg ggattttcca aaaaccgcgc
                                                                         60
```

tagogoccaa attgggattt tocaaaaago ogaaattggg attttocaaa aacogoogat ogocogocco gttgaogoaa atgggoggta ggogtgtaog gtgggaggtt tatataagoa gagotogttt agtgaacogt cagatoagat ot	120 180 212
<210> 43 <211> 96 <212> DNA <213> Artificial Sequence	
<220> <223> engineered regulatory sequence	
<400> 43 gctagccccg ccccgttgac gcaaatgggc ggtaggcgtg tacggtggga ggtctatata agcagagctc gtttagtgaa ccgtcagatc agatct	60 96
<210> 44 <211> 154 <212> DNA <213> Artificial Sequence	
<220> <223> engineered regulatory sequence	
<400> 44 gctagcgccc aggtcgggat tttccgagga gccgaggtcg ggattttccg aggaccgccg atcgcccgcc ccgttgacgc aaatgggcgg taggcgtgta cggtgggagg cctatataag cagagctcgt ttagtgaacc gtcagatcag atct	60 120 154
<210> 45 <211> 154 <212> DNA <213> Artificial Sequence	
<220> <223> engineered regulatory sequence	
<400> 45 gctagcgccc aggtcgggat tttccgagga gccgaggtcg ggattttccg aggaccgccg atcgcccgcc ccgttgacgc aaatgggcgg taggcgtgta cggtgggagg cctatataag cagagctcgt ttagtgaacc gtcagatcag atct	60 120 154
<210> 46 <211> 762 <212> DNA <213> Artificial Sequence	
<220> <223> engineered promoter construct	
<pre><400> 46 ggtacctcaa tattggccat tagccatatt attcattggt tatatagcat aaattaatat tggctattgg ccattgcata cgttgtatct atatcataat atgtacattt atattggctc atgtccaata tgaccgccat gttggcattg attattgact agttattaat agtaatcaat tacggggtca ttagttcata gcccatatat ggagttccgc gttacataac ttacggtaaa tggcccgcct ggctgaccgc ccaacgaccc ccgcccattg acgtcaataa tgacgtatgt tcccatagta acgcaaatag ggattttcca ttaacgtcaa tgggtggagt atttacggta</pre>	120 180 240 300 360

```
aactgcccac ttggcagtac atcaagtgta tcatatgcca agtccgcccc ctattgacgt
                                                                       420
caatgacggt aaatggcccg cctggcatta tgcccagtac atgactttat gggattttcc
                                                                       480
tatttggcag tacatctacg tattagtcat cgctattacc atggtgatgc ggttttggca
                                                                       540
gtacaccaat gggcgtggat agcggtttga ctcacgggga tttccaagtc tccacccat
                                                                       600
tgacgtcaat gggagtttgt tttggcacca aggtaaaagg gattttccaa aatgtcgtaa
                                                                       660
caactgcgat cgcccgccc gttgacgcaa atgggcggta ggcqtqtacg gtgggaggtt
                                                                       720
tatataagca gagctcgttt agtgaaccgt cagatcaagc tt
                                                                       762
<210> 47
<211> 762
<212> DNA
<213> Artificial Sequence
<220>
<223> engineered promoter construct
<400> 47
ggtacctcaa tattggccat tagccatatt attcattggt tatatagcat aaattaatat
                                                                        60
tggctattgg ccattgcata cgttgtatct atatcataat atgtacattt atattggctc
                                                                       120
atgtccaata tgaccgccat gttggcattg attattgact agttattaat agtaatcaat
                                                                       180
tacggggtca ttagttcata gcccatatat ggagttccgc gttacataac ttacggtaaa
                                                                       240
tggcccgcct ggctgaccgc ccaacgaccc ccgcccattg acgtcaataa tgacgtatgt
                                                                       300
tcccatagta acgcaaatat tcccgggaaa ttaacgtcaa tgggtggagt atttacggta
                                                                       360
aactqcccac ttqqcaqtac atcaaqtqta tcatatqcca aqtccqcccc ctattqacqt
                                                                       420
caatgacggt aaatggcccg cctggcatta tgcccagtac atgactttat tctcgaggaa
                                                                       480
tatttggcag tacatctacg tattagtcat cgctattacc atggtgatgc ggttttggca
                                                                       540
                                                                       600
gtacaccaat gggcgtggat agcggtttga ctcacgggga tttccaagtc tccacccat
tgacgtcaat gggagtttgt tttggcacca aggtaaaatt acgcgtaaaa aatgtcgtaa
                                                                       660
caactqcqat cgcccqcccc qttgacgcaa atgggcggta ggcgtgtacg gtgggaggtt
                                                                       720
gctagccgca gagctcgttt agtgaaccgt cagatcaagc tt
                                                                       762
<210> 48
<211> 762
<212> DNA
<213> Artificial Sequence
<220>
<223> engineered promoter construct
<400> 48
ggtacctcaa tattggccat tagccatatt attcattggt tatatagcat aaatcaatat
                                                                        60
                                                                       120
tggctattgg ccattgcata cgttgtatct atatcataat atgtacattt atattggctc
atgtccaata tgaccgccat gttggcattg attattgact agttattaat agtaatcaat
                                                                       180
tacggggtca ttaqttcata gcccatatat ggagttccgc gttacataac ttacggtaaa
                                                                       240
                                                                       300
tggcccqcct ggctgaccqc ccaacqaccc ccgcccattq acqtcaataa tgacqtatqt
tcccatagta acgccaatag ggactttcca ttgacgtcaa tgggtggagt atttacggta
                                                                       360
aactgcccac ttggcagtac atcaagtgta tcatatgcca agtccgcccc ctattgacgt
                                                                       420
caatgacggt aaatggcccg cctggcatta tgcccagtac atgaccttac gggactttcc
                                                                       480
tacttggcag tacatctacg tattagtcat cgctattacc atggtgatgc ggttttggca
                                                                       540
gtacaccaat qqqcqtqqat aqcqqtttqa ctcacqqqqa tttccaaqtc tccacccat
                                                                       600
tgacgtcaat gggagtttgt tttggcacca aaatcaacgg gactttccaa aatgtcgtaa
                                                                       660
caactgcgat cgcccgccc gttgacgcaa atgggcggta ggcgtgtacg gtgggaggtc
                                                                       720
tatataagca gagctcgttt agtgaaccgt cagatcaagc tt
                                                                       762
<210> 49
<211> 12
<212> DNA
```

<213> Artificial Sequence	
<220> <223> wild type regulatory sequence	
<400> 49 gactgtttgt tt	.2
<210> 50 <211> 12 <212> DNA <213> Artificial Sequence	
<220> <223> wild type regulatory sequence	
<400> 50 aggactcttg ga	.2
<210> 51 <211> 46 <212> DNA <213> Artificial Sequence	
<220> <223> wild type regulatory sequence	
<400> 51 tactaggagg ctgtaggcat aaattggtct gcgcaccagc accatg 4	6
<210> 52 <211> 46 <212> DNA <213> Artificial Sequence	
<220> <223> engineered regulatory sequence	
<400> 52 tactaggagg ctgtaggcat aaattagtct gcgcaccagc accatg 4	6
<210> 53 <211> 46 <212> DNA <213> Artificial Sequence	
<220> <223> engineered regulatory sequence	
<400> 53 tactaggatt agtgcttaag cccttggtct gcgcaccagc accatg 4	ć
<210> 54 <211> 46 <212> DNA <213> Artificial Sequence	

<220> <223>	engineered regulatory sequence	
<400> tactac	54 ggagg ctgtaggcat aaagctcgag tatacaacgc accatg	46
<210><211><211><212><213>	50	
<220> <223>	engineered regulatory sequence	
<400> tactac		50
<210> <211> <212> <213>	50	
<220> <223>	engineered regulatory sequence	
<400> tactac		50
<210><211><211><212><213>	50	
<220> <223>	engineered regulatory sequence	
<400> tactag		50
<210><211><211><212><213>	51	
<220> <223>	engineered regulatory sequence	
<400> accttg		51
<210><211><211><212><213>	51	
<220>	engineered regulatory sequence	

```
<400> 59
  accttgaggc atacttcaaa gactgtttat tttaataacg ggaggagttg g
                                                                          51
  <210> 60
  <211> 51
  <212> DNA
  <213> Artificial Sequence
  <220>
  <223> engineered regulatory sequence
  <400> 60
  accttgaggc atacttcaaa gactgtttat ttaaggactg ggaggagttg g
                                                                          51
  <210> 61
  <211> 6513
  <212> DNA
  <213> Artificial Sequence
  <220>
  <223> heterologous nucleic acid construct
  <400> 61
  tcaatattgg ccattagcca tattattcat tggttatata gcataaatca atattggcta
                                                                          60
  ttggccattg catacgttgt atctatatca taatatgtac atttatattg gctcatgtcc
                                                                         120
  aatatgaccg ccatgttggc attgattatt gactagttat taatagtaat caattacggg
                                                                         180
  qtcattaqtt catagcccat atatggagtt ccgcgttaca taacttacgg taaatggccc
                                                                         240
  gcctggctga ccgcccaacg acccccqccc attgacqtca ataatgacqt atgttcccat
                                                                         300
  agtaacgcca atagggactt tccattgacg tcaatgggtg gagtatttac ggtaaactgc
                                                                         360
  ccacttggca gtacatcaag tgtatcatat gccaagtccg ccccctattg acgtcaatga
                                                                         420
  cggtaaatgg cccgcctggc attatgccca gtacatgacc ttacgggact ttcctacttg
                                                                         480
  gcagtacatc tacgtattag tcatcgctat taccatggtg atgcggtttt ggcagtacac
                                                                         540
  caatgggcgt ggatagcggt ttgactcacg gggatttcca agtctccacc ccattgacgt
                                                                         600
  caatgggagt ttgttttggc accaaaatca acgggacttt ccaaaatgtc gtaacaactg
                                                                         660
                                                                         720
n cgatcgcccg ccccgttgac gcaaatgggc ggtaggcgtg tacggtggga ggtctatata
  agcagagete qtttagtgaa eegteagate actagaaget ttattgeggt agtttateae
                                                                         780
  agttaaattg ctaacgcagt cagtgcttct gacacaacag tctcgaactt aagctgcagt
                                                                         840
                                                                         900
  gactetetta aggtageett geagaagttg gtegtgagge aetgggeagg taagtateaa
  ggttacaaga caggtttaag gagaccaata gaaactgggc ttgtcgagac agagaagact
                                                                         960
  cttgcgtttc tgataggcac ctattggtct tactgacatc cactttgcct ttctctccac
                                                                        1020
 aggtgtccac tcccagttca attacagctc ttaaggctag agtacttaat acgactcact
                                                                        1080
  ataggctage cagettgaag caagecteet gaaagatgga ggegtegetg eeggeecagg
                                                                        1140
 ccgccgagac ggaggaggtg ggtcttttcg tcgaaaaata cctccggtcc gatgtcgcgc
                                                                        1200
 cggcggaaat tgtcgcgctc atgcgcaacc tcaacagcct gatgggacgc acgcggttta
                                                                        1260
  tttacctggc gttgctggag gcctgtctcc gcgttcccat ggccacccgc agcagcgcca
                                                                        1320
 tatttcggcg gatctatgac cactacgcca cgggcgtcat ccccacgatc aacgtcaccg
                                                                        1380
 gagagetgga getegtggee etgecececa ecetgaaegt aacceeegte tgggagetgt
                                                                        1440
 tgtgcctgtg cagcaccatg gccgcgccc tqcattgqqa ctcggcggcc ggqggatctq
                                                                        1500
 ggaggacctt cggccccgat gacgtgctqq acctactqac cccccactac qaccqctaca
                                                                        1560
 tgcagctggt gttcgaactg ggccactgta acgtaaccga cggacttctg ctctcggagg
                                                                        1620
 aagccgtcaa gcgcgtcgcc gacgccctaa gcggctgtcc cccgcgcggg tccgttagcg
                                                                        1680
 agacggacca cgcggtggcg ctgttcaaga taatctgggg cgaactgttt ggcgtgcaga
                                                                        1740
 tggccaaaag cacgcagacg tttcccgggg cgggggcgt taaaaaacctc accaaacaga
                                                                        1800
 caatcgtggg gttgttggac gcccaccaca tcgaccacag cgcctgccgg acccacaggc
                                                                        1860
 agctgtacgc cctgcttatg gcccacaagc qqqaqtttqc gggcqcqcgc ttcaagctac
                                                                        1920
 gcgtgcccgc gtgggggcgc tgtttgcgca cgcactcatc cagcgccaac cccaacgctg
                                                                        1980
```

acatcatcct	ggaggcggcg	ctgtcggagc	tccccaccga	ggcctggccc	atgatgcagg	2040
gggcggtgaa	ctttagcacc	ctaatgaagc	tactgtcttc	tatcgaacaa	gcatgcccaa	2100
	aaaggtagat					2160
gcctggggga	cgagctccac	ttagacggcg	aggacgtggc	gatggcgcat	gccgacgcgc	2220
tagacgattt	cgatctggac	atgttggggg	acggggattc	cccgggtccg	ggatcgccag	2280
	acttgacgcg					2340
	cctttagtga					2400
	aaccacaact					2460
	tttatttgta					2520
	tatgtttcag					2580
	atgtggtaaa					2640
	tagcggcgca					2700
	agcgccctag					2760
	tttccccgtc					2820
	cacctcgacc					2880
	tagacggttt					2940
	caaactggaa					3000
	ccgatttcgg					3060
	aacaaaatat					3120
						3180
	gtggaatgtg					3240
	gcaaagcatg					
	aggcagaagt					3300
	tccgcccatc					3360
	aattttttt					3420
	gtgaggaggc					3480
	agtctcgaac					3540
	ccggccgctt					3600
	tctgatgccg					3660
	gacctgtccg					3720
	acgacgggcg					3780
	ctgctattgg					3840
	aaagtatcca					3900
	ccattcgacc					3960
	cttgtcgatc					4020
	gccaggctca					4080
	tgcttgccga					4140
	ctgggtgtgg					4200
tgctgaagag	cttggcggcg	aatgggctga	ccgcttcctc	gtgctttacg	gtatcgccgc	4260
	cagcgcatcg					4320
ctggggttcg	aaatgaccga	ccaagcgacg	cccaacctgc	catcacgatg	gccgcaataa	4380
aatatcttta	ttttcattac	atctgtgtgt	tggttttttg	tgtgaagatc	cgcgtatggt	4440
gcactctcag	tacaatctgc	tctgatgccg	catagttaag	ccagccccga	cacccgccaa	4500
cacccgctga	cgcgccctga	cgggcttgtc	tgctcccggc	atccgcttac	agacaagctg	4560
tgaccgtctc	cgggagctgc	atgtgtcaga	ggttttcacc	gtcatcaccg	aaacgcgcga	4620
	cctcgtgata					4680
	aggtggcact					4740
	ttcaaatatg					4800
	aaggaagagt					4860
	ttgccttcct					4920
	gttgggtgca					4980
	ttttcgcccc					5040
	ggtattatcc				_	5100
	gaatgacttg					5160
	aagagaatta					5220
	gacaacgatc					5280
	aactcgcctt					5340
	caccacgatg					5400
gagegega	Jacquegaeg	Julytaytaa	cygodacaac	guuguguaa	Juliance	2400

gcgaactact tactctagct tcccggcaac aattaataga ctggatggag gcggataaaq 5460 ttgcaggacc acttctgcgc tcggcccttc cggctggctg gtttattgct gataaatctg 5520 gagccggtga gcgtgggtct cgcggtatca ttgcagcact ggggccagat ggtaagccct 5580 cccgtatcgt agttatctac acqacqqqqa qtcaqqcaac tatqqatqaa cqaaataqac 5640 agatcgctga gataggtgcc tcactgatta agcattggta actgtcagac caagtttact 5700 catatatact ttaqattqat ttaaaacttc atttttaatt taaaaqqatc taqqtqaaqa 5760 tootttttga taatotoatg accaaaatco ottaacgtga gttttcgtto cactgagcgt 5820 cagaccccgt agaaaagatc aaaggatctt cttgagatcc tttttttctg cgcgtaatct 5880 gctgcttgca aacaaaaaa ccaccgctac cagcggtggt ttgtttgccg gatcaaqaqc 5940 taccaactct ttttccgaag gtaactggct tcagcagagc gcagatacca aatactgtcc 6000 ttctagtgta gccgtagtta ggccaccact tcaagaactc tgtagcaccg cctacatacc 6060 tegetetget aateetgtta ceagtggetg etgecagtgg egataagteg tgtettaceg 6120 ggttggactc aagacgatag ttaccggata aggcgcagcg gtcgggctga acggggggtt 6180 cgtgcacaca gcccagcttg gagcgaacga cctacaccga actgagatac ctacagcgtg 6240 agctatgaga aagcgccacg cttcccgaag ggagaaaggc ggacaggtat ccggtaagcg 6300 gcagggtcgg aacaggagag cgcacgaggg agcttccagg gggaaacgcc tggtatcttt 6360 atagteetgt egggtttege cacetetgae ttgagegteg atttttgtga tgetegteag 6420 ggggggggag cctatggaaa aacgccagca acgcggcctt tttacqqttc ctqqcctttt 6480 gctggccttt tgctcacatg gctcgacaga tct 6513 <210> 62 <211> 6439 <212> DNA <213> Artificial Sequence

<220>

<223> heterologous nucleic acid construct

<400> 62

tcaatattgg ccattagcca tattattcat tggttatata gcataaatca atattggcta 60 ttggccattg catacgttgt atctatatca taatatgtac atttatattg gctcatgtcc 120 aatatgaccg ccatgttggc attgattatt gactagttat taatagtaat caattacggg 180 gtcattagtt catagcccat atatggagtt ccgcgttaca taacttacgg taaatggccc 240 gcctggctga ccgcccaacg acccccgccc attgacgtca ataatgacgt atgttcccat 300 agtaacgcca atagggactt tccattgacg tcaatgggtg gagtatttac ggtaaactgc 360 ccacttggca gtacatcaag tgtatcatat gccaagtccg cccctattg acgtcaatga 420 cggtaaatgg cccgcctggc attatgccca gtacatgacc ttacgggact ttcctacttg 480 gcagtacatc tacgtattag tcatcgctat taccatggtg atgcggtttt ggcagtacac 540 caatgggcgt ggatagcggt ttgactcacg gggatttcca agtctccacc ccattgacgt 600 caatgggagt ttgttttggc accaaaatca acgggacttt ccaaaatgtc gtaacaactg 660 cgatcgcccg ccccgttgac gcaaatgggc ggtaggcgtg tacggtggga ggtctatata 720 agcagagete gtttagtgaa eegteagate actagaaget ttattgeggt agtttateae 780 agttaaattg ctaacqcagt cagtgcttct gacacaacag tctcgaactt aagctgcagt 840 gactctctta aggtagcctt gcagaagttg gtcgtgaggc actgggcagg taagtatcaa 900 ggttacaaga caggtttaag gagaccaata gaaactgggc ttgtcgagac agagaagact 960 cttgcgtttc tgataggcac ctattggtct tactgacatc cactttgcct ttctctccac 1020 aggtgtccac tcccagttca attacagctc ttaaggctag agtacttaat acgactcact 1080 ataggctagc cagcttgaag caagcctcct gaaagatgga ggcgtcgctg ccggcccagg 1140 ccgccgagac ggaggaggtg ggtcttttcg tcgaaaaata cctccggtcc gatgtcgcgc 1200 cggcggaaat tgtcgcgctc atgcgcaacc tcaacagcct gatgggacgc acgcggttta 1260 tttacctggc gttgctggag gcctgtctcc gcgttcccat ggccacccgc agcagcgcca 1320 tattteggeg gatetatgae caetaegeea egggegteat eeceaegate aaegteaeeg 1380 gagagetgga getegtggee etgeeeccea ceetgaaegt aacceeegte tgggagetgt 1440 tgtgcctgtg cagcaccatg gccgcgccc tgcattggga ctcggcggcc gggggatctg 1500 ggaggacctt cggccccgat gacgtgctgg acctactgac ccccactac gaccgctaca 1560 tgcagctggt gttcgaactg ggccactgta acgtaaccga cggacttctg ctctcgqagq 1620 aageegteaa gegegtegee gaegeeetaa geggetgtee eeegegeggg teegttageg 1680

agacggacca	cgcggtggcg	ctgttcaaga	taatctgggg	cgaactgttt	ggcgtgcaga	1740
			cggggcgcgt			1800
			tcgaccacag			1860
			gggagtttgc			1920
			cgcactcatc			1980
			tccccaccga			2040
			agaagagaaa			2100
			gggaggagtg			2160
			agaactataa			2220
			ggtacctgaa			2280
			ataagataca			2340
			atttgtgaaa			2400
			gttaacaaca			2460
			ttttaaagca			2520
			cctgaatggc			2580
			acgcgcacgt			2640
			cttcctttct			2700
			tagggttccg			2760
			gttcacgtag			2820
			cgttctttaa			2880
			attcttttga			2940
			tttaacaaaa			3000
			accttctgag			3060
			ccaggctccc			3120
			tgtggaaagt			3180
			tcagcaacca			3240 3300
			gcccattctc			3360
			teggeetetg			3420
			aaaaagcttg			3480
			aacaagatgg actgggcaca			3540
			ggcgcccggt			3600
			aggcagcgcg			3660
			ttgtcactga			3720
			tgtcatctca			3780
			tgcatacgct			3840
			gagcacgtac			3900
			aggggctcgc			3960
			atctcgtcgt			4020
			tttctggatt			4080
			tggctacccg			4140
		-	tttacggtat			4200
			tcttctgagc			4260
			acgatggccg			4320
			aagatccgcg			4380
			ccccgacacc			4440
			gcttacagac			4500
			tcaccgaaac			4560
			atgataataa			4620
			cctatttgtt			4680
			tgataaatgc			4740
			gcccttattc			4800
			gtgaaagtaa			4860
			ctcaacagcg			4920
cgccccgaag	aacgttttcc	aatgatgagc	acttttaaag	ttctgctatg	tggcgcggta	4980
ttatcccgta	ttgacgccgg	gcaagagcaa	ctcggtcgcc	gcatacacta	ttctcagaat	5040
gacttggttg	agtactcacc	agtcacagaa	aagcatctta	cggatggcat	gacagtaaga	5100



gaattatgca	gtgctgccat	aaccatgagt	gataacactg	cggccaactt	acttctgaca	5160
acgatcggag	gaccgaagga	gctaaccgct	tttttgcaca	acatggggga	tcatgtaact	5220
cgccttgatc	gttgggaacc	ggagctgaat	gaagccatac	caaacgacga	gcgtgacacc	5280
acgatgcctg	tagcaatggc	aacaacgttg	cgcaaactat	taactggcga	actacttact	5340
ctagcttccc	ggcaacaatt	aatagactgg	atggaggcgg	ataaagttgc	aggaccactt	5400
ctgcgctcgg	cccttccggc	tggctggttt	attgctgata	aatctggagc	cggtgagcgt	5460
gggtctcgcg	gtatcattgc	agcactgggg	ccagatggta	agccctcccg	tatcgtagtt	5520
atctacacga	cggggagtca	ggcaactatg	gatgaacgaa	atagacagat	cgctgagata	5580
ggtgcctcac	tgattaagca	ttggtaactg	tcagaccaag	tttactcata	tatactttag	5640
attgatttaa	aacttcattt	ttaatttaaa	aggatctagg	tgaagatcct	ttttgataat	5700
ctcatgacca	aaatccctta	acgtgagttt	tcgttccact	gagcgtcaga	ccccgtagaa	5760
aagatcaaag	gatcttcttg	agatcctttt	tttctgcgcg	taatctgctg	cttgcaaaca	5820
aaaaaaccac	cgctaccagc	ggtggtttgt	ttgccggatc	aagagctacc	aactctttt	5880
ccgaaggtaa	ctggcttcag	cagagcgcag	ataccaaata	ctgtccttct	agtgtagccg	5940
tagttaggcc	accacttcaa	gaactctgta	gcaccgccta	catacctcgc	tctgctaatc	6000
ctgttaccag	tggctgctgc	cagtggcgat	aagtcgtgtc	ttaccgggtt	ggactcaaga	6060
			ggctgaacgg			6120
agcttggagc	gaacgaccta	caccgaactg	agatacctac	agcgtgagct	atgagaaagc	6180
			aggtatccgg			6240
ggagagcgca	cgagggagct	tccaggggga	aacgcctggt	atctttatag	tcctgtcggg	6300
			ttgtgatgct			6360
tggaaaaacg	ccagcaacgc	ggccttttta	cggttcctgg	ccttttgctg	gccttttgct	6420
cacatggctc	gacagatct					6439